

## CLAIMS

What is claimed:

1. A method for treating or preventing a tumor necrosis factor-mediated disease in an individual in need thereof comprising co-administering methotrexate and a TNF $\alpha$  antagonist to said individual, in therapeutically effective amounts.
2. A method of Claim 1 wherein said TNF $\alpha$  antagonist and methotrexate are administered simultaneously.
3. A method of Claim 1 wherein said TNF $\alpha$  antagonist and methotrexate are administered sequentially.
4. A method of Claim 1 wherein the tumor necrosis factor-mediated disease is selected from the group consisting of: autoimmune disease, acute or chronic immune disease, inflammatory disease and neurodegenerative disease.
5. A method of Claim 4 wherein said TNF $\alpha$  antagonist is administered in multiple doses.
6. A method of Claim 1 wherein said TNF $\alpha$  antagonist prevents or inhibits TNF $\alpha$  synthesis or TNF $\alpha$  release.
7. A method of Claim 6 wherein said TNF $\alpha$  antagonist is a phosphodiesterase inhibitor.
8. A method of Claim 7 wherein said phosphodiesterase inhibitor is selected from the group consisting of: pentoxifylline and rolipram.
9. A method of Claim 6 wherein said TNF $\alpha$  antagonist is selected from the group consisting of: thalidomide and tenidap.

10. A method of Claim 6 wherein said TNF $\alpha$  antagonist is selected from the group consisting of: a A2b adenosine receptor agonist and a A2b adenosine receptor enhancer.
- 5 11. A method of Claim 5 wherein said TNF $\alpha$  antagonist is an anti-TNF $\alpha$  antibody or antigen-binding fragment thereof.
12. A method of Claim 11 wherein said anti-TNF $\alpha$  antibody or antigen-binding fragment is a chimeric antibody or chimeric fragment, wherein said chimeric antibody or chimeric fragment comprises a non-human variable region specific for TNF $\alpha$  or an antigen-binding portion thereof and a human constant region.
- 10 13. A method of Claim 12 wherein said chimeric antibody binds to one or more epitopes included in amino acid residues set forth in SEQ ID NO:1 or SEQ ID NO:2.
14. A method of Claim 13 wherein said chimeric antibody competitively inhibits binding of TNF $\alpha$  to monoclonal antibody cA2.
- 15 15. A method of Claim 13 wherein said chimeric antibody is monoclonal antibody cA2.
16. A method of Claim 11 wherein said anti-TNF $\alpha$  antibody is a humanized antibody or antigen-binding fragment thereof.
- 20 17. A method of Claim 16 wherein said humanized antibody binds to one or more epitopes included in amino acid residues set forth in SEQ ID NO:1 or SEQ ID NO:2.
18. A method of Claim 11 wherein said anti-TNF $\alpha$  antibody is a resurfaced antibody or antigen-binding fragment thereof.
- 25 19. A method of Claim 18 wherein said resurfaced antibody binds to one or more epitopes included in amino acid residues set forth in SEQ ID NO:1 or SEQ ID NO:2.

20. A method of Claim 5 wherein said TNF $\alpha$  antagonist is a soluble TNF $\alpha$  receptor or functional portion thereof.
21. A method of Claim 20 wherein said soluble TNF $\alpha$  receptor is selected from the group consisting of: p55 TNF $\alpha$  receptor and p75 TNF $\alpha$  receptor.
- 5 22. A method of Claim 20 wherein said soluble TNF $\alpha$  receptor is a TNF $\alpha$  receptor multimeric molecule.
23. A method of Claim 20 wherein said soluble TNF $\alpha$  receptor is a TNF $\alpha$  receptor immunoreceptor fusion molecule.
- 10 24. A method for treating or preventing arthritis in an individual in need thereof comprising co-administering methotrexate and a TNF $\alpha$  antagonist to said individual, in therapeutically effective amounts.
25. A method of Claim 24 wherein said TNF $\alpha$  antagonist and methotrexate are administered simultaneously.
- 15 26. A method of Claim 24 wherein said TNF $\alpha$  antagonist and methotrexate are administered sequentially.
27. A method of Claim 24 wherein said TNF $\alpha$  antagonist is administered in multiple doses.
28. A method of Claim 24 wherein said TNF $\alpha$  antagonist prevents or inhibits TNF $\alpha$  synthesis or TNF $\alpha$  release.
- 20 29. A method for treating or preventing rheumatoid arthritis in an individual in need thereof comprising co-administering methotrexate and a TNF $\alpha$  antagonist to said individual, in therapeutically effective amounts.
30. A method of Claim 29 wherein said TNF $\alpha$  antagonist and methotrexate are administered simultaneously.

31. A method of Claim 29 wherein said TNF $\alpha$  antagonist and methotrexate are administered sequentially.
32. A method of Claim 29 wherein said TNF $\alpha$  antagonist is administered in multiple doses.
- 5 33. A method of Claim 29 wherein said TNF $\alpha$  antagonist prevents or inhibits TNF $\alpha$  synthesis or TNF $\alpha$  release.
34. A method for treating or preventing Crohn's disease in an individual in need thereof comprising co-administering methotrexate a TNF $\alpha$  antagonist to said individual, in therapeutically effective amounts.
- 10 35. A method of Claim 34 wherein said TNF $\alpha$  antagonist and methotrexate are administered simultaneously.
36. A method of Claim 34 wherein said TNF $\alpha$  antagonist and methotrexate are administered sequentially.
- 15 37. A method of Claim 34 wherein said TNF $\alpha$  antagonist is administered in multiple doses.
38. A method of Claim 34 wherein said TNF $\alpha$  antagonist prevents or inhibits TNF $\alpha$  synthesis or TNF $\alpha$  release.